

**MODULATORS OF THE HYPOCRETIN SYSTEM AND**  
**METHODS OF SCREENING THEREFOR**

**ABSTRACT OF THE DISCLOSURE**

Methods for modulating the hypocretin system, as well as methods for identifying compounds that act as hypocretin-system modulators are provided. In modulating the hypocretin system, the method comprises administering a therapeutically effective amount of a preprohypocretin-expression modulator to an individual, wherein the preprohypocretin-expression modulator alters preprohypocretin expression in preprohypocretin-expressing cells. The method for identifying compounds comprises contacting a test compound to cells equipped with the 5' flanking promoter of the preprohypocretin gene operably linked to a nucleic acid sequence and determining whether the test compound alters transcription of the nucleic acid sequence in the cell, wherein the test compound's ability to alter transcription is indicative of a compound that modulates the hypocretin system. The invention also provides compounds, pharmaceutical compositions, nucleic acid sequences, expression vectors, transformed host cells, and the like for carrying out the methods.